RATIONALE FOR THE DEVELOPMENT OF ONTARIO AIR STANDARDS FOR FORMALDEHYDE

CONSULTATION DRAFT

February 1998

Standards Development Branch
Ontario Ministry of the Environment

Ontario

Acknowledgement

This document was produced by staff of Standards Development Branch. Particular thanks are extended to Dr. Angela Li-Muller for her contribution to the risk assessment component of the document.

Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan which was released in October 1996, identified candidate substances for the development of air standards for the next several years (MOEE, 1996). Formaldehyde was identified as a priority for review based both on its pattern of use in Ontario and recent toxicological information published since the existing standards were developed in 1970 and reassessed in 1982. This document examines standards and guidelines for formaldehyde used in other jurisdictions and their scientific basis and recommends that the existing Ambient Air Quality Criterion (AAQC) and point of impingement (POI) standard for formaldehyde in Ontario remain unchanged from their present values.

Formaldehyde is a naturally occurring organic chemical which is a normal metabolite produced in many living organisms. A major source of formaldehyde in urban air is emissions from incomplete burning of petroleum fuels, especially from vehicle exhaust. Industries that produce and use formaldehyde also contribute to outdoor air levels. Levels of formaldehyde measured in rural areas are typically below 1 $\mu g/m^3$. The annual average concentrations in urban areas typically range from 2 to 10 $\mu g/m^3$, with short-term peaks being reported as much as ten times the annual average.

Formaldehyde induces both cancer and non-cancer effects. The non-cancer effects observed in humans include odour (unpleasant smell), irritation of the eyes, nose and respiratory tract. On a cellular level, formaldehyde causes tissue damage and stimulates cell division and tissue growth. Formaldehyde is classified as a probable human carcinogen by the International Agency for Research on Cancer and the United States Environmental Protection Agency. In developing air standards, it is necessary to consider both the carcinogenic and non-carcinogenic effects of this compound.

Ontario currently has a half-hour Point of Impingement (POI) standard in regulation 346 and a 1-hour Ambient Air Quality Criterion (AAQC) of 65 $\mu g/m^3$ for formaldehyde (MOEE, 1994a). The standards are based on odour and irritation effects in humans. Based on recent toxicological information, these standards, originally developed in 1970 and reassessed 1982, are now in need of review.

In developing air quality standards for Ontario, the Ministry of the Environment is reviewing and considering air quality guidelines and standards used by leading agencies world-wide. In evaluating current toxicological information and the guidelines and standards of several other agencies which consider both the carcinogenic and non-carcinogenic effects, the Ministry has concluded that the current Ontario air standards for formaldehyde are protective of human health for both types of effects.

Based on an assessment of ambient air quality guidelines used in major jurisdictions worldwide, the levels of formaldehyde measured in Ontario, modeled ground level concentrations from recent applications for Certificates of Approval, the Ministry of the Environment recommends:

- the existing Ambient Air Quality Criterion for formaldehyde remains unchanged from its present value of 65 µg/m^3 (micrograms of formaldehyde per cubic metre of air) but that the averaging time be changed from 1-hour to 24-hours to reflect the fact that the AAQC is protective against chronic health effects as well as odour and irritation;

- the existing 1/2-hour point of impingement standard for formaldehyde listed in Regulation 346 remain unchanged from its current level of 65 µg/m^3.

Table of Contents

Acknowledgement i

Executive Summary ii

1.0 Introduction 1

2.0 Review and Evaluation 2
2.1 General Information 2
2.2 Sources and Levels 3
2.3 Review of Existing Air Quality Regulations 4

3.0 Development of an Ambient Air Quality Criteria for Ontario 6
3.1 Consideration of Odour/Irritation Effects 6
3.2 Consideration of Carcinogenicity 6
3.2.1 Potential for Inducing Cancer 6
3.2.1 Approaches to Evaluate Formaldehyde Carcinogenic Risk 7
3.2.3 Population Risk from Exposure to Formaldehyde 9
3.3 Recommendations for an Ambient Air Quality Criterion for Formaldehyde 11

4.0 Status of Stakeholder Consultations 12

5.0 Recommendations 12

6.0 References 12

7.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines 19
7.1 Agency-Specific Summary: Federal Government of the United States 19
7.2 Agency-Specific Summary: State of California 23
7.3 Agency-Specific Summary: World Health Organization 27
7.4 Agency-Specific Summary: The Netherlands 30
7.5 Agency-Specific Summary: Swedish Institute of Environmental Medicine 32
7.6 Agency-Specific Summary: New York State 34
7.7 Agency-Specific Summary: State of Massachusetts 36

1.0 Introduction

Ontario's primary approach to regulating air emissions is based on achieving and maintaining air quality which is protective of human health and the environment. The *Environmental Protection Act* requires all stationary sources which emit or have the potential to emit a contaminant to obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

Compliance with air quality standards and guidelines is one of the criteria used to issue Certificates of Approval. Sources or potential sources of a contaminant are required to control emissions to ensure that the concentration of a contaminant specified by the standard is not exceeded at any point beyond their property. Dispersion modelling which incorporates detailed engineering calculations is used to relate emission rates from a source to resulting ambient concentrations of a particular contaminant.

The Ministry of the Environment uses a combination of regulatory standards, ambient air quality criteria (AAQCs) and point of impingement (POI) guidelines in reviewing Certificates of Approval (MOEE, 1994a). Point of impingement standards are established under Regulation 346 and can be used directly as enforcement tools as the regulation specifies that a source cannot emit a contaminant at a level which would result in a standard being exceeded at its maximal point of impingement off its property (Section 5(3)). All sources are required to comply with Regulation 346 point of impingement standards unless they are specifically exempted in regulation. As point of impingement standards specified under Regulation 346 apply to all sources, socio-economic issues need to be taken into consideration in their development to ensure that the standards are technically feasible and there is a balance between the benefits and costs of improved ambient air quality.

In addition to point of impingement standards established under Regulation 346, the Ministry also has a larger number of ambient air quality criteria and point of impingement guidelines which are derived from AAQCs. These are used by the Ministry to assess general air quality and to evaluate the *potential* for causing an adverse effect (MOEE 1994). Like point of impingement standards specified in Regulation 346, point of impingement guidelines are also used in Certificates of Approval to approve new and modified emission sources. Once incorporated into a legal instrument like a Certificate of Approval, point of impingement guidelines are legally binding, however unlike Regulation 346 point of impingement standards, they do not automatically apply to existing sources at the time they are promulgated. AAQCs are normally set at a level not expected to cause adverse human health or environmental effects based on continuous exposure. As such, socio-economic factors such as technical feasibility and costs are not explicitly considered when establishing such limits.

Generally, point of impingement standards and guidelines which employ half-hour averaging times are set such that compliance with the standard or guideline will ensure that the Ambient Air

Quality Criterion which is based on longer term averaging periods (e.g. 24-hours) will be met. In certain cases where the effect can result from short-term exposures, like odours, the 24-hour Ambient Air Quality Criterion and the half-hour point of impingement standard may have the same value.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan which was released in October 1996, identified candidate substances for the development of air standards for the next several years. Formaldehyde was identified as a priority for review based both on its pattern of use in Ontario and recent toxicological information published since the existing standards were developed in 1970 and reassessed in 1982. This document provides the scientific rationale for the ambient air quality criterion and point of impingement standard for formaldehyde.

2.0 Review and Evaluation

2.1 General Information

Formaldehyde, (chemical structure HCHO) is a colourless gas with a strong characteristic odour. The Chemical Abstracts Service (CAS) identification number is 50-00-0, the Registry of Toxic Effects of Chemical Substances (RTECS) number is LP8925000, and the United Nations Hazardous Material numbers for aqueous formaldehyde solutions are 1198 and 2209. Formaldehyde is also known as formalin, methyl aldehyde, formic aldehyde, methylene oxide, methanal, and oxomethane.

Formaldehyde is a naturally occurring chemical. It is present in most living organisms as an intermediate in the production of several essential chemicals (e.g., some amino acids, lipids, and nucleotide) and as a degradation product from the natural metabolic breakdown of amino acids. As a result, the blood levels in humans, monkeys, and rats are about 2 to 3 mg/L and appear to be unaffected by respiratory exposure (IARC, 1995).

Formaldehyde is widely used in a variety of industrial and commercial products and processes (Consensus Panel, 1984; ACGIH, 1991). It is usually sold as a commercial product in the form of an aqueous solution containing 30-50% formaldehyde and up to 15% methanol as a stabilizer.

The America Council of Governmental Industrial Hygienists (ACGIH, 1991) has reviewed and discussed the information presented by the U.S. National Research Council (NRC, 1981) and the World Health Organization (WHO, 1989). This information indicates that reported odour detection thresholds for formaldehyde range from 60 to 1,200 $\mu g/m^3$ (0.05 to 1.0 ppm), that neurophysiological responses (e.g. increased nasal mucous flow) begin to occur in the range of 60 to 1,440 $\mu g/m^3$ (0.05 to 1.2 ppm), and that eye irritation begins to occur in the range of 12 to 2,200 $\mu g/m^3$ (0.01 to 2 ppm). Results from studies employing exposure levels in the range of 12 to 60 $\mu g/m^3$ (0.01 to 0.05 ppm) are equivocal. For example, eye irritation experienced at 12

$\mu g/m^3$ could be attributed to the presence of other chemicals which may have contributed to the response. Irritation of the upper respiratory passages (nose and throat) has been reported to occur at an air concentration ranging between 120 and 13,200 $\mu g/m^3$ (0.1 to 11 ppm). Irritation of the eyes and respiratory tract tends to increase in severity with increasing exposure concentrations. The variability in these responses is at least in part due to uncertainties in the exposure concentrations, the possible presence of other chemicals in the exposure air, differences in the determination of what constitutes a response, as well as natural variations in the sensitivity of the exposed population. For example, children are thought to be more sensitive than adults (WHO, 1987; ACGIH, 1991). WHO (1987) employed an odour threshold of 100 $\mu g/m^3$ (0.08 ppm) and an eye irritation threshold of 500 $\mu g/m^3$ (0.42 ppm) as working values.

Formaldehyde is considered to be a Class B1 carcinogen (probable human carcinogen, based on limited evidence in humans and sufficient evidence in animals) by the US EPA (1995). It is classified as a 2A carcinogen, i.e. a probable human carcinogen (sufficient evidence for animals, limited evidence for humans) by the International Agency for Research on Cancer (IARC, 1987, 1995).

2.2 Sources and Levels

Formaldehyde is naturally present in the air resulting from the cycling of methane through the environment. In Canada, the major industrial source of formaldehyde emission to the atmosphere arises from the wood industries, accounting for 66.7% of total air emission reported in 1995 (NPRI, 1995). Other important sources include discharges from industries that produce chemical and chemical products, non-metallic mineral product, as well as paper and allied products.

The 1995 National Pollutants Release Inventory (NPRI, 1995) listed 34 sources of formaldehyde in Ontario with a total release of 163.8 tonnes to the atmosphere. The 1995 reported figures represent a slight increase in the number of sources and the level of emission over the 1994 figures (NPRI, 1994, 1995). The vast majority of these releases came from the chemical and nonmetallic mineral industries.

An analysis of recent applications for Certificates of Approval in Ontario identified 75 Certificates covering emission of formaldehyde to the atmosphere. Although the majority of these approvals are for emissions from paint spray operations, quite a number cover exhaust from fume hoods of chemical and medical laboratories. The median Ground Level Concentration (GLC) predicted by Regulation 346 dispersion modelling for all 75 sources was approximately 4 $\mu g/m^3$ with 2 of the sources having GLCs above 65 $\mu g/m^3$. The maximum and minimum Ground Level Concentrations predicted were 89 $\mu g/m^3$ and 0.0002 $\mu g/m^3$, respectively.

In general, the background levels of formaldehyde in the outdoor air in uncontaminated areas have been reported to be in the range of 0.14 to 0.96 $\mu g/m^3$ (0.12 to 0.8 ppb; ACGIH, 1991). The levels are generally higher in the urban centres, about 2 to 4 $\mu g/m^3$ for major Canadian cities

including Vancouver, Windsor, Toronto, Ottawa, Montreal (MOEE 1994b). Reported annual average concentrations vary from about 1.8 to 6.1 µg/m^3 at various monitoring sites (Windsor, Toronto and Ottawa) in Ontario between 1990 and 1994 (Steer, 1997). These levels are generally lower than the typical annual average of approximately 5 to 10 µg/m^3 in urban areas around the world (WHO, 1987; California EPA, 1992a) and are below the current Ontario AAQC of 65 µg/m^3. Spurs of concentration peaks, which could be as much as 10 times higher than the annual average levels, can occur over short durations during periods of peak traffic activity or smog incidents in urban areas. Nevertheless, the maximum levels measured at monitoring stations in Windsor, Toronto and Ottawa between 1990 and 1994 (5.0-31.2 µg/m^3; Steer, 1997) did not exceed the current half-hour point of impingement standard.

A substantial portion of the increased levels in urban areas results from the photochemical degradation of atmospheric hydrocarbons which are products of incomplete combustion of petroleum fuels. Levels can be higher in areas where industrial processes use formaldehyde. Indoor air levels in homes and offices are often higher than the outdoor ambient levels, due to the presence of formaldehyde in various products (plastic, plywood, textiles, carpets, household chemicals etc.), and in tobacco smoke (ACGIH, 1991). The mean indoor levels in conventional homes with no urea-formaldehyde foam insulation were reported to be 25-60 µg/m^3 (Preuss, *et al.* 1985).

2.3 Review of Existing Air Quality Regulations

Agency-specific summaries of information concerning air quality guidelines for formaldehyde are presented in the Appendix. Table 1 provides a brief summary of this information. The basis for Ontario's current ambient air quality criterion of 65 µg/m^3 (1-hour average) was presented in Harding (1982). Although an irritation threshold of 130 µg/m^3 (100 ppb) was reported, the lower value of 65 µg/m^3 (50 ppb), the odour threshold value, was used as the basis for the AAQC. The value of 65 µg/m^3 (50 ppb) also corresponded to the half-hour point of impingement (POI) standard in Regulation 346 (R.R.O. 1990).

Table 1. Summary of Existing Air Quality Guidelines[1] for Formaldehyde

Agency, Date[2]	Guideline(s)		Comments
U.S. EPA[4] (IRIS) 1987	No ambient air exposure limits available.		
	0.8 µg/m^3 0.08 µg/m^3	(lifetime exposure) (lifetime exposure)	$1*10^{-5}$ additional cancer risk $1*10^{-6}$ additional cancer risk Based on a unit risk of $1.3*10^{-5}$ (µg/m^3)$^{-1}$
California 1992	370 µg/m^3 3.6 µg/m^3	(1-hour average) (annual average)	Acute and chronic reference levels derived from odour, irritation and occupational exposure limits.
	0.17 µg/m^3	(lifetime exposure)	$1*10^{-6}$ additional cancer risk based on a unit risk of $6*10^{-6}$ (µg/m^3)$^{-1}$
WHO 1996	100 µg/m^3 10 µg/m^3	(½ hour average) (½ hour average)	Based on odour and irritation. For hypersensitive persons.
Netherlands 1987	100 µg/m^3 40 µg/m^3 30 µg/m^3	(1-hour average) (99.99 percentile) (24-hour average) (98 percentile) (24-hour average) (95 percentile)	Based on risk assessment documents in Dutch, appear to be for non-cancer endpoints (odour and irritation)
Sweden[3] 1993	120 µg/m^3 12 to 60 µg/m^3	(1-hour average) (annual average)	Based on application of safety factors of 10 and 100 to the irritation threshold. Considered to represent a low cancer risk.
New York 1990	30 µg/m^3	(1-hour average)	1-hour average is derived from occupational exposure limits.
	0.06 µg/m^3	(annual average)	$1*10^{-6}$ additional cancer risk estimate.
Massachusetts 1990	0.33 µg/m^3	(24-hour average)	24-hour average is derived from occupational exposure limits.
	0.08 µg/m^3	(annual average)	$1*10^{-6}$ additional cancer risk based on a unit risk of $1.3*10^{-5}$ (µg/m^3)$^{-1}$
Ontario (Current) 1982	65 µg/m^3 65 µg/m^3	(½-hour point of impingement limit) (1-hour average AAQC)	Air quality standards based on odour/irritation considerations.

1. Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
2. Date here refers to when the health-based guideline background report or original legislative initiative was issued. Sources were the respective agency documents.
3. Proposed by the Swedish Institute of Environmental Medicine.
4. The USEPA has developed a revised unit risk value for formaldehyde (1991) which has not yet been incorporated into IRIS.
5. 1 ppm ~ 1.2 mg/m^3 at 20-25°C

3.0 Development of an Ambient Air Quality Criteria for Ontario

There are two basic approaches employed in developing ambient air quality guidelines for formaldehyde, those based on the prevention of odour/irritant effects (WHO, Netherlands, Sweden) and those based on suspected carcinogenicity of formaldehyde (New York, Massachusetts, US EPA, California). The current Ontario AAQC belongs to the first type. The two approaches are discussed below.

3.1 Consideration of Odour/Irritation Effects

On short term exposure, non-cancer human responses start with an odour threshold of about 0.1 mg/m^3 (0.08 ppm) (reported range 60 to 1,200 $\mu g/m^3$), progressing to eye and upper respiratory (nose, throat) irritation at 0.5 mg/m^3 (0.42 ppm). Irritation and discomfort increase sharply at 1-20 mg/m^3 (0.8-17 ppm) and death may occur at 30 mg/m^3 (25 ppm) or higher (reviewed by Consensus Panel, 1984; WHO, 1987; ACGIH, 1991; IARC, 1995). Sensory irritation can be demonstrated in animals which can be accompanied by cytotoxicity and an increase in cell proliferation the respiratory tract after acute and chronic exposure to increased levels (Chang *et al.* 1983; Swenberg *et al.* 1983; Monticello *et al.* 1989, 1991, 1996). The threshold for cell proliferation and tissue damage in otherwise undamaged nasal mucosa in rodents and monkeys has been identified to be 2.5 mg/m^3 (2.1 ppm) of inhaled formaldehyde (IARC, 1995). Although data on induction of cell proliferation are not available for humans, the current air standards that are based on odour/irritation, including the Ontario value (65 $\mu g/m^3$; 0.05 ppm), are likely to be below the threshold for cell proliferation in the respiratory tract in humans.

Several agencies had developed air quality guidelines for formaldehyde based on odour/irritation (Table 1). Guidelines based on a one-year averaging period include: 3.6 $\mu g/m^3$ (California), and 12 to 60 $\mu g/m^3$ (Sweden). Shorter-term guidelines (½- to 24-hour averaging periods) include: 0.33 $\mu g/m^3$ (Massachusetts), 30 $\mu g/m^3$ (New York), 30 to 100 $\mu g/m^3$ (Netherlands), 100 $\mu g/m^3$ (WHO), 120 $\mu g/m^3$ (Sweden), and 370 $\mu g/m^3$ (California).

3.2 Consideration of Carcinogenicity

3.2.1 Potential for Inducing Cancer

With respect to carcinogenicity, IARC (1987) and US EPA (1987) have reviewed essentially the same literature and both classified formaldehyde as a probable human carcinogen according to their individual weight-of-evidence classification scheme. The basis consists of (1) limited human evidence for an association of formaldehyde exposure with cancer of the nose and nasopharynx at occupational exposure levels; (2) sufficient evidence from multiple inhalation studies in animal demonstrating nasal cancers; and (3) consideration of other key evidence. The latter information includes (1) known genotoxic activity of formaldehyde including the formation of DNA adducts and (2) the ability of formaldehyde to injure cells and induce cell division. On the other hand, data

based on epidemiological studies on exposed individuals failed to provide evidence for a causal association between formaldehyde exposure and human cancer incidence (UAREP, 1988; McLaughlin, 1994). These findings are consistent with the evaluation of US EPA (1987) and IARC (1987) which considered that the epidemiological data did not provide "sufficient" evidence for carcinogenicity in humans. In October, 1994, the IARC working group reassessed all the epidemiological data and analyses including the most recent Iron Foundry study (Andjelkovich *et al.* 1995). Although their interpretation of one major study differed from that of McLaughlin (1994), their overall conclusion remained the same: "limited" evidence of causal relationship in humans. Taking into consideration evidence from experimental animals and other relevant evidence (discussed above) the IARC working group (1995) reconfirmed their assessment and has classified formaldehyde as a probable human carcinogen (Group 2A). Therefore, it is necessary to develop air standards for formaldehyde with due consideration for both carcinogenic and non-carcinogenic effects of this compound.

3.2.1 Approaches to Evaluate Formaldehyde Carcinogenic Risk

Threshold Versus Non-threshold

The existing carcinogenicity-based air standards (New York, Massachusetts) are developed by either adopting the risk assessment conducted by US EPA (1987) or using similar methodologies. The US EPA 1987 assessment assumed formaldehyde-induced carcinogenicity was due to a non-threshold mechanism and thus used the linearized multistage model (LMM) to extrapolate tumour response from high to low dose. Empirically, the airborne concentration showed a nonlinear relationship with nasal squamous cell carcinoma incidence in the 2-year chronic inhalation rat studies (Kerns *et al.* 1983; Monticello *et al.* 1996), with limited cancer development at low dose levels followed by a steep disproportionate increase in response above certain concentration (no increase at 2 ppm, a 1% incidence at 6 ppm, and a 50% incidence at 15 ppm, equivalent to a 2.5 fold increase in dose resulting in a 50-fold increase in tumours). Such observation suggests the possibility of a carcinogenic threshold for formaldehyde.

Unlike many biological and toxic endpoints such as odour and irritation against which organisms are believed to have a certain tolerance (hence the presence of a threshold), carcinogenic response is more complex. For contaminants considered to be cancer initiators, i.e. chemicals that cause neoplastic cellular transformation by inducing mutation or DNA lesion through direct interaction with the DNA, the outcome is probabilistic in nature and no threshold is expected. On the other hand, non-genotoxic carcinogens act by mechanisms which do not involve direct interaction of the chemicals or their metabolites with the DNA, and a threshold could be in operation. Promoters that induce cell proliferation belong to the latter class of chemicals. Although attempts have been made to identify with reasonable certainty the presence/absence of a threshold for carcinogens epidemiologically and experimentally using known genotoxic carcinogens (reviewed by Zeise *et al.* 1987; Purchase and Auton, 1995), they were not successful. The difficulty lies on the lack of statistical power due to inadequate sample size especially at low doses. These studies lead to the

conclusion that it is impossible to determine the presence/absence of a carcinogenic threshold based on experimental observation only and the selection of risk assessment methodology (threshold versus non-threshold) has to be based on an understanding of the mechanism of toxicity (Purchase and Auton, 1995).

Mechanistic Consideration

Although a lot has been learned about the mechanism of formaldehyde carcinogenicity through extensive research by the Chemical Industry Institute of Toxicology (CIIT; reviewed in Conolly *et al.* 1995), it does not appear that a definitive conclusion or consensus has been reached for the presence/absence of a carcinogenic threshold for formaldehyde. The following paragraphs present a discussion on what is known and arguments for and against the presence of a carcinogenic threshold based on mechanistic consideration.

Formaldehyde induces cell proliferation and the cell proliferation concentration-response on chronic exposure correlates well with the concentration-response for tumour formation in the nasal passages of rats in a two year bioassay (Monticello, 1996). Due to the clear site-specificity of formaldehyde-induced nasal cancer, a regional approach was taken for the comparison of cell proliferation and tumour response. No increase in cell proliferation over the controls and no tumours were observed at 0.7 and 2 ppm. In contrast, a great increase in both responses were observed at 10 and 15 ppm. In the 6-ppm group, no increase in cell proliferation was detected and only a single animal developed nasal squamous cell carcinoma. It has to be noted, however, that other acute and subchronic studies (Casanova *et al.* 1994; Monticello *et al.* 1991) reported significant increase in cell proliferation at 6 ppm. The observation suggests that cell proliferation plays an important role in the development of the observed nasal squamous cell carcinomas at 10 and 15 ppm and the risk of malignant transformation is greatly reduced at concentrations below the threshold for formaldehyde-induced nasal cell proliferation (2 ppm or 2.5 mg/m^3). The ability of formaldehyde to enhance cytotoxicity and cell proliferation is consistent with its demonstrated cancer promotion potential (Cosma and Marchok, 1987; Iversen, 1986). On the other hand, formaldehyde is known to induce mutation and genotoxic events in a variety of experimental systems including rodents *in vivo* and human cells *in vitro* (reviewed in IARC, 1995). DNA-protein cross-links (DPX) are formed in a curvilinear manner (increasing disproportionately at high levels) when inhaled formaldehyde reaches the nuclei of target nasal epithelial cells in rodents and monkeys, indicative of direct interaction with DNA (Casanova *et al.* 1989; 1994). These cross-links could lead to mutagenicity and play a critical role in the induction of tumours by formaldehyde (Conolly *et al.* 1995). Therefore, there is a possibility that formaldehyde could also be a potential "initiator".

At high levels of exposure, the carcinogenicity of formaldehyde correlates well with both DNA-protein crosslinks and induced cell replication in the exposed rats (Casanova *et al.*, 1989, 1994; Monticello, 1996). Both mechanisms, genotoxic effect and cell proliferation, could be operating, possibly synergistically, at such high exposure levels resulting in sharp convexity while genotoxic

effect may (or may not) operate alone at low levels (US EPA, 1991). While there is a consensus among scientists that formaldehyde-induced cell damage and compensatory cell proliferation contribute significantly to cancer effects at high concentrations, whether there is a potential for increased formaldehyde-induced cancer risk below the threshold for cell proliferation remains controversial (Squire and Cameron, 1984; US EPA, 1991; California EPA, 1992b; IARC, 1995; Swenberg *et al.* 1995; Conolly *et al.* 1995). The supporters of the carcinogenic threshold hypothesis refer to the failure to establish a definitive causal relationship between cancer and occupational exposure, the absence of evidence of initiation in *in vivo* initiation-promotion studies using mouse skin, and the apparent prerequisite of increased cell proliferation for cancer risk in rodents (discussed in Squire and Cameron, 1984; McLaughlin, 1994). On the other hand, California Air Resources Board (1992b) did not consider the evidence for carcinogenic threshold credible for formaldehyde. Even in the presence of protective trapping and removal function of mucociliary apparatus, enzymatic detoxification, and DNA repair processes, which greatly reduce the effect of formaldehyde interacting with the DNA of the nasal mucosa, substantial DNA-protein crosslinks were identified at concentration as low as 0.3 ppm (below the observed threshold for cell proliferation) in the rat nose (Casanova *et al.* 1989). Because formaldehyde is a known genotoxin and mutagen and has been shown to interact with DNA at such low concentration, the California Air Resources Board decided to embrace the non-threshold assumption for formaldehyde-induced carcinogenicity. Whether the mutagenicity of DNA protein cross-links is dependent on the induction of cell proliferation remains to be further explored (Conolly *et al.* 1995). If enhanced cell proliferation in the presence of DNA-protein cross-links is indeed the mechanism by which mutation and subsequent transformation of a normal cell to a neoplastic cell is induced, even though formaldehyde is present in the environment at levels below its cell proliferation threshold, the presence of another cell proliferator (which is often present in the environment) would allow the expression of the mutagenic events arising from formaldehyde-induced DNA-protein crosslinks.

3.2.3 Population Risk from Exposure to Formaldehyde

While the controversy of the presence/absence of threshold in formaldehyde-induced carcinogenicity cannot be easily resolved at present, one could observe that the typical environmental levels and the current Ontario AAQC are well below the concentration range at which cell proliferation is enhanced. No increased risk due to the promotion effects (considered to have a threshold) of formaldehyde would be expected at these levels. On the other hand, increased cancer risk due to the initiation potential (considered not to have a threshold) at the environmental levels would have to be estimated. The nonlinear dose response relationship for the cancer induction of both a weak genotoxin and a promoter like formaldehyde can only be adequately modelled using a biologically based model of the type developed by Moolgavkar and Knudson (1981). However, a lack of definitive mechanistic data does not allow such an effort. Up to the present, the existing risk assessments have used the linearized multistage model (LMM) (US EPA, 1987, 1991; Starr, 1990; California EPA, 1992b) to predict carcinogenic response at low doses from known responses at high doses. Extrapolation using the LMM (that assumes

linearity at low doses) from a dose at which genotoxic effects and cell proliferation induction likely act synergistically results in an overestimate of risk at environmental levels due to genotoxic effects alone. However, the observed non-linearity of the dose response curve can be reduced by fitting empirically to the LMM the rat tumour data versus target tissue levels (levels of DNA-protein crosslink formation). Using the levels of DNA-protein crosslink formation as a surrogate for target tissue levels accounts for the pharmacokinetic non-linearity due to the protective action of the mucociliary apparatus and enzymatic detoxification. Although use of target tissue levels in the modelling is unable to account for the non-linearity due to pharmacodynamics (e.g. effect of enhanced cell proliferation), the uncertainty of the risk assessment is greatly reduced. Therefore, risk assessments (US EPA, 1991; California EPA, 1992b) that input levels of DNA-protein crosslinks (as surrogates for target tissue levels) in the modelling are more relevant than assessments that input airborne concentrations (US EPA, 1987 and recorded in IRIS). The US EPA assessment update (1991) differs from the California EPA (1992b) assessment which used a body surface (default) scaling factor to extrapolate cancer risk from rats to humans. This extrapolation method results in attributing higher risk to larger animals exposed to the same dosage. The result is contrary to the observation that the level of DNA-protein crosslinks induced in the corresponding nasal epithelium in monkeys was lower than that in rats at the same formaldehyde exposure concentration (Casanova *et al.* 1991), which suggests that monkeys are at a lower risk than rats at the same concentration. On the contrary, US EPA (1991) used the monkey DNA-protein crosslink data as a surrogate for human target tissue dose in the assessment on the basis that the anatomy and breathing patterns of humans were similar to those of the monkeys. The dosimetry differences between rodents and primates are accounted for and the corresponding uncertainty is further reduced in the assessment.

Table 2 shows the incremental cancer risk due to daily exposure to formaldehyde over a lifetime under typical environmental levels using the results of the US EPA modelling efforts which assumes linearity at low doses (US EPA 1991 - though not yet published and finalized for incorporation into their IRIS database, this assessment uses biomarkers as indicators for exposure and is considered more representative than the US EPA's 1987 assessment). Based on this assessment, lifetime exposure at existing ambient levels as well as the current AAQC (converted to an annual average equivalent concentration using a conversion factor of 5 (MOEE 1994c)), results in an incremental cancer risk estimate in the range generally considered negligible (most likelihood estimate for lifetime exposure to 13 $\mu g/m^3$ ~ 2×10^{-8}; 95% upper bound estimate ~ 4×10^{-6}). Considering the possibility of overestimation of risk as discussed above, one can conclude that the current Ontario AAQC is sufficiently protective of the population against carcinogenic risk due to airborne formaldehyde exposure. Since formaldehyde is a highly water soluble and extremely reactive chemical, it is unlikely that it will produce effects remote from the site of release (Owen *et al.* 1990). Further, absorption by the skin does not result in significant amount of formaldehyde in the bloodstream and almost all intake through ingestion is excreted (WHO, 1987). Therefore, it is reasonable to assume that in setting air standard for formaldehyde, it should not be necessary to consider the effects of exposure from pathways other than inhalation.

Table 2. Estimated incremental cancer risk due to lifetime exposure to formaldehyde using the US EPA (1991) risk assessment methodology

Scenario	Concentration µg/m^3 (ppm)	MLE[a]	UCL[b]
Rural areas	0.14 - 0.96 (0.0001-0.0008)[c,d]	0 - 3 x 10^{-11}	4 x 10^{-8} - 3 x 10^{-7}
Urban centres	5 - 10 (0.004-0.008)[d,e]	7 x 10^{-10} - 3 x 10^{-9}	1 x 10^{-6} - 3 x 10^{-6}
Canadian cities	2 - 4 (0.002-0.003)[d,f]	2 x 10^{-10} - 4 x 10^{-10}	7 x 10^{-7} - 1 x 10^{-6}
Ontario cities (Windsor)	up to 31.2 (0.03)[f]	up to 4 x 10^{-8}	up to 9 x 10^{-6}
AAQC	65 13[g]	1 x 10^{-7} 2 x 10^{-8}	2 x 10^{-5} 4 x 10^{-6}

[a]most likelihood estimate
[b]95 % upper bound estimate
[c]ACGIH (1991)
[d]annual average
[e]WHO (1987), California EPA (1992a)
[f] Steer (1997)
[g] converted to an annual average equivalent using a conversion factor of 5

3.3 Recommendations for an Ambient Air Quality Criterion for Formaldehyde

Recommendations for new or revised Ontario Ambient Air Quality Criteria (AAQC) and point of impingement (POI) standards are based upon a weight-of-evidence evaluation of available information. In assessing air quality standards for formaldehyde, the ministry evaluated the existing ambient air quality criterion in light of standards and guidelines used in other jurisdictions which are based on both carcinogenicity and non-carcinogenic end-points. The Ministry also considered recent scientific information concerning the toxicity of formaldehyde and its mechanism of action.

In evaluating this information, the Ministry has concluded that the existing ambient air quality criterion and point of impingement standard are protective of public health against both short-term effects (odour irritation) and chronic effects (tissue damage, cancer). On this basis, the Ministry is recommending that the existing AAQC and point of impingement standard remain unchanged from their present values of 65 µg/m^3 (Table 3). However, the Ministry is recommending that the averaging time for the Ambient Air Quality Criterion for formaldehyde be changed from 1-hour to 24-hours to reflect the fact that it is based on the prevention of chronic effects resulting from longer-term exposure. The half-hour average point of impingement standard is based on odour irritation effects.

Table 3: Recommended AAQC and POI Standard for Formaldehyde		
AAQC	24-hour Average	65 µg/m^3
Reg 346 POI Standard	½-hour Average	65 µg/m^3

While the ambient air quality criterion for formaldehyde of 65 µg/m^3 is based on the prevention of adverse health effects in the human population, the potential effect of formaldehyde on other terrestrial biota including plants, soil microbes and wildlife was also examined. Limited field and laboratory studies, plus additional modelling efforts suggest that exposures to formaldehyde at the AAQC level will not be detrimental to both vegetation and wildlife in Ontario.

4.0 Status of Stakeholder Consultations

In January 1997, the Ministry initiated limited stakeholder consultation on the initial suite of 14 proposed air standards developed under the Ministry's Standards Plan. The purpose of these consultations was to seek comments from Ontario sources and other stakeholders on the standards proposed. During the course of these consultations no specific concerns were identified with respect to the proposed standard for formaldehyde.

5.0 Recommendations

- The Ministry of the Environment proposes that the existing Ambient Air Quality Criterion for formaldehyde remain unchanged from its present value of 65 µg/m^3 but that the averaging time be changed from 1-hour to 24-hours to reflect the fact that the AAQC is protective of the Ontario population against chronic health effects as well as odour and irritation.

- The Ministry of the Environment proposes that the existing half-hour Point of Impingement Standard listed for formaldehyde in Regulation 346 remain unchanged form its current level of 65 µg/m^3. The point of impingement standard is based on the odour/irritation effects of formaldehyde.

6.0 References

ACGIH, 1991. Documentation Of The Threshold Limit Values for Substances in Workroom Air (6th ed.). American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH.

Andjelkovich, D.A., D.B. Janzen, R.B. Conolly, and F.J. Miller, 1995. Formaldehyde Exposure Not Associated with Cancer of the Respiratory Tract in Iron Foundry Workers: a Synopsis of CIIT Epidemiologic Findings. CIIT Activities 5:1-9.

Blair, A., P.A. Stewart, M. O'Berg, W. Gaffey, J. Walrath, J. Ward, R. Bales, S. Kaplan, and D. Cubit, 1986. Mortality among Industrial Workers Exposed to Formaldehyde. J. Natl. Cancer Inst. 76: 1071-1084.

Blair, A., P. Stewart, P.A. Hoover, and J.F. Fraumeni, 1987. Cancers of the Nasopharynx and Oropharynx and Formaldehyde Exposure. J. Natl. Cancer Inst. 78: 191-193.

California EPA, 1992a. Final Report on the Identification of Formaldehyde as a Toxic Air Contaminant. Part A Exposure Assessment. Technical Support Document. California Environmental Protection Agency, Air Resources Board, Sacramento CA. 89 p.

California EPA, 1992b. Final Report on the Identification of Formaldehyde as a Toxic Air Contaminant. Part B Health Assessment. Technical Support Document. California Environmental Protection Agency, Air Resources Board, Sacramento CA. 25 p.

CAPCOA, 1993. Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

Casanova, M., D.F. Deyo and H.d'A. Heck, 1989. Covalent Binding of Inhaled Formaldehyde to DNA in the Nasal Mucosa of Fischer 344 rats: Analysis of Formaldehyde and DNA by High-Performance Liquid Chromatography and Provisional Pharmacokinetics Interpretation. Fundam. Appl. Toxicol. 12: 397-417.

Casanova, M., K.T. Morgan, W.H. Steinhagen, J.I. Everitt, J.A. Popp, and H. d'A.Heck, 1991. Covalent Binding of Inhaled Formaldehyde to DNA in the Respiratory Tract of Rhesus Monkeys: Pharmacokinetics, Rat-to-Monkey Inter-Species Scaling, and Extrapolation to Man. Fundam. Appl. Toxicol. 17: 409-428.

Casanova, M., K.T. Morgan, E.A. Gross, O.R. Moss and H.d'A. Heck, 1994. DNA-Protein Cross-Links and Cell Replication at Specific Sites in the Nose of F344 Rats Exposed Subchronically to Formaldehyde. Fundam. Appl. Toxicol. 23: 525-536.

Chang, J.C.F., E.A. Gross, J.A. Swenberg and C.S. Barrow, 1983. Nasal Cavity Deposition, Histopathology, and Cell Proliferation after Single or Repeated Formaldehyde Exposures in B6C3F1 Mice and F-344 Rats. Toxicol. Appl. Pharmacol. 68: 161-176.

Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston MA.

Conolly, R.B., D.D. Andjelkovich, M. Casanova, H.d'A. Heck, D.B. Janszen, J.S. Kimbell, K.T. Morgan and L. Recio, 1995. Multidisciplinary, Iterative Examination of the Mechanism of Formaldehyde Carcinogenicity: The Basis for Better Risk Assessment. CIIT Activities 15: 1-11.

Consensus Panel, 1984. Report on the Consensus Workshop on Formaldehyde. Environ. Health Perspect. 58: 323-381.

Cosma, G.N. and A.C. Marchok, 1987. The Induction of Growth Altered Cell Population (Tumour-Initiation Sites) in Rat Tracheal Implants Exposed to Benzo[a]pyrene and Formaldehyde. Carcinogenesis 8: 1951-1953.

Harding, D.H., 1982. Health Effects of Formaldehyde. Occupational Health in Ontario, Volume 3, Number 2 (April, 1982): 64-80.

IARC, 1995. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 62. Wood Dust and Formaldehyde. International Agency for Research on Cancer, Lyon, France.

IARC, 1987. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Genetic and Related Effects: An Updating of Selected IARC Monographs from Volumes 1 to 42. Supplement 6. International Agency for Research on Cancer, Lyon, France. 697+ p.

IARC, 1982. ARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Volumes 1 to 29. Supplement 4. International Agency for Research on Cancer, Lyon, France.

Iversen, O.H., 1986. Formaldehyde and Skin Carcinogenesis. Environ. Int. 12: 541-544.

Kerns, W.D., K.L. Pavkov, D.J. Donofrio, E.J. Gralla and J.A. Swenberg, 1983. Carcinogenicity of Formaldehyde in Rats and Mice after Long-Term Inhalation Exposure. Cancer Res. 43: 4382-4392.

Lewis, D.C. and G.V. Alexeeff, 1989. Quantitative Risk Assessment of Non-cancer Health Effects for Acute Exposure to Air Pollutants. In: Proceedings of the Air and Waste Management Association 82nd Annual Meeting. June 1989, Vol. 89-91.4: 1-11.

McConnell, E.E., 1995. Historical Review of the Rodent Bioassay and Future Directions. Reg. Toxicol. Pharmacol. 21: 38-43.

McLaughlin, J.K., 1994. Formaldehyde and Cancer: a Critical Review. Int. Arch. Occup. Environ. Health 66: 295-301.

MOEE, 1996. Three Year Plan for Standard-Setting. Ministry of Environment and Energy, Toronto, Ontario.

MOEE, 1994a. Summary of Point of Impingement Standards, Ambient Air Quality Criteria (AAQCs) and Approvals Screening Levels (ASLs). Standards Development Branch, Ontario Ministry of the Environment and Energy, Toronto, Ontario.

MOEE, 1994b. Windsor Air Quality Study. Prepared for the Windsor Air Quality Committee by the Ontario Ministry of the Environment and Energy, Toronto, Ontario.

MOEE, 1994c. Rationale for the Development of Soil, Drinking Water and Air Quality Criteria for Lead. Ministry of Environment and Energy, Toronto, Ont.

Monticello, T.M., F.J. Miller, and K.T. Morgan, 1991. Regional Increases in Rat Nasal Epithelial Cell Proliferation Following Acute and Subchronic Inhalation of Formaldehyde. Toxicol. Appl. Pharmacol. 111: 409-421.

Monticello, T.M., K.T. Morgan, J.I. Everitt and J.A. Popp, 1989. Effects of Formaldehyde Gas on the Respiratory Tract of Rhesus Monkeys. Am. J. Pathol. 134: 515-527.

Monticello, T.M., J.A. Swenberg, E.A. Gross, J.R. Leininger, J.S. Kimbell, S. Seilkop, T.B. Starr, J.E. Gibson and K.T. Morgan, 1996. Correlation of Regional and Nonlinear Formaldehyde-Induced Nasal Cancer with Proliferating Populations of Cells. Cancer Res. 56: 1012-1022.

Moolgavkar, S.H. and A.G.Jr. Knudson, 1981. Mutation and Cancer: A Model for Human carcinogenesis. J. Natl. Cancer Inst. 66: 1037-1052.

NPRI, 1995. The National Pollutants Release Inventory: Summary Report and Database of 1995. Canadian Environment Protection Act. Environment Canada.

NPRI, 1994. The National Pollutants Release Inventory: Summary Report and Database of 1994. Canadian Environment Protection Act. Environment Canada.

NRC, 1981. National Research Council, Committee on Aldehydes, Board on Toxicology and Environmental Health Hazards. National Academy Press, Washington, DC, as cited in ACGIH, 1991.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulations Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A Review of Environmental Quality Objectives and Their Policy Framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 p.

New York State DEC, 1991. New York State Air Guideline -1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation (DEC), Albany, New York NY. 20 p. + Appendices.

New York State DOH, 1990. Formaldehyde Health Assessment. Division of Environmental Health, Bureau of Toxic Substance Assessment (Cover letter only).

Owen, B.A., C.S. Dudney, E.L. Tan and C.E. Easterly, 1990. Formaldehyde in Drinking Water: Comparative Hazard Evaluation and an Approach to Regulation. Regulat. Toxicol. Pharmacol. 11: 220-236.

Preuss, P.W., R.L. Dailey and E.S. Lehman, 1985. Exposure to Formaldehyde. In: Turoski, C., ed. Formaldehyde. Analytical Chemistry and Toxicology. Advances in Chemistry Series, Vol 210, Washington DC, American Chemical Society, pp.247-259. Cited in ARC, 1995.

Purchase, I.F.H. and T.R. Auton, 1995. Thresholds in Chemical Carcinogenesis. Regulatory Toxicol. Pharmacol. 22: 199-205.

Sellakumar, A.R., C.A. Snyder, J.J. Solomon, and E.R. Albert, 1985. Carcinogenicity of Formaldehyde and Hydrogen Chloride in Rats. Toxicol. Appl. Pharmacol. 81: 401-406.

Squire, R.A. and L.L. Cameron, 1984. An Analysis of Potential Carcinogenic Risk from Formaldehyde. Regulatory Toxicol. Pharmacol. 4: 107-129.

Starr, T.B., 1990. Quantitative Cancer Risk Estimation for Formaldehyde. Risk Anal. 10: 85-91.

Stayner, L.T., L. Elliott, L. Blade, R. Keenlyside and W. Halperin, 1988. A retrospective Cohort Mortality Study of Workers Exposed to Formaldehyde in the Garment Industry. Am. J. Ind. Med. 13: 667-682.

Steer, P., 1997. Personal Communication. Data obtained from T. Dann, Environment Canada.

Swenberg, J.A., C.S. Barrow, C.J. Boreiko, H.d'A. Heck, R.J. Levine, K.T. Morgan and T.B. Starr, 1983. Non-Linear Biological Responses to Formaldehyde and Their Implications for Carcinogenic Risk Assessment. Carcinogenesis 4: 945-952.

Swenberg, J.A., W.D. Kerns, R.I. Mitchell, E.J. Gralla, and K.L. Pavkov, 1980. Induction of Squamous Cell Carcinomas of the Rat Nasal Cavity by Inhalation Exposure to Formaldehyde Vapor. Cancer Res. 40: 3398-3402.

Swenberg, J.A., D.K. La, N.A. Scheller and K.-y. Wu, 1995. Dose-Response Relationships for Carcinogens. Toxicol. Letters 82/83: 751-756.

Tobe, M., T. Kaneko, Y. Uchida, E. Kamata, Y. Ogawa, Y. Ikeda, and M. Saito, 1985. Studies of the Inhalation Toxicity of Formaldehyde. National Sanitary and Medical Laboratory Service (Japan). 94 p.

U.S. EPA, 1987. Assessment of Health Risks to Garment Workers and Certain Home Residents from Exposure to Formaldehyde. U.S. Environmental Protection Agency, Office of Toxic Substances, Washington DC.

U.S. EPA, 1991. Formaldehyde Risk Assessment Update: Final Draft, June 11, 1991. U.S. Environmental Protection Agency, Office of Toxic Substances, Washington DC. 154 p. + appendices.

U.S. EPA, 1993. Motor Vehicle-Related Air Toxics Study. Emission Planning and Strategies Division, Office of Air and Radiation. U.S. Environmental Protection Agency, Washington DC.
U.S. EPA, 1995. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington DC.

Universities Associated for Research and Education in Pathology, Inc. (UAREP), 1988. Epidemiology of Chronic Occupational Exposure to Formaldehyde: Report of the Ad Hoc Panel on Health Aspects of Formaldehyde. Toxicol. Indust. Health 4: 77-90.

Vaughan, T.L., C. Strader, S. Davis, and J.R. Daling, 1986. Formaldehyde and Cancers of the Pharynx, Sinus and Nasal Cavity: i. Occupational Exposures. Int. J. Cancer. 38: 677-683.

Vaughan, T.L., C. Strader, S. Davis, and J.R. Daling, 1986. Formaldehyde and Cancers of the Pharynx, Sinus and Nasal Cavity: ii. Residential Exposures. Int. J. Cancer. 38: 685-688.

Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. Chemosphere 27: 1691-1706.

World Health Organization (WHO), 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark. 426 p.

WHO, 1989. Formaldehyde. Environmental Health Criteria No. 89. World Health Organization, Geneva, Switzerland, as cited in ACGIH, 1991).

WHO, 1996. Updating and Revision of the Air Quality Guidelines for Europe. Report on a WHO Working Group on Volatile Organic Compounds, Brussels, Belgium, 2-6 October, 1995. WHO Regional Office for Europe, Denmark. 22p.

Zeise, L., R. Wilson and E.A.C. Crouch, 1987. Dose Response Relationships for Carcinogenesis: A Review. Environ. Health Perspect. 73: 259-308.

7.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

7.1 Agency-Specific Summary: Federal Government of the United States

1. Name of Chemical: Formaldehyde

2. Agency: U.S. Environmental Protection Agency

3. Guideline Value(s):
No ambient air exposure limits are currently promulgated. As of the current date (March, 1998), the IRIS database has not reported a reference concentration (RfC) for chronic inhalation exposure. However, there are quantitative estimates of carcinogenic risk from inhalation exposure. The inhalation unit risk reported in IRIS is $1.3 * 10^{-5}$ $(\mu g/m^3)^{-1}$, representing an additional risk of 1 in 100,000 and 1 in 1,000,000 for a lifetime exposure to 0.8 $\mu g/m^3$ and 0.08 $\mu g/m^3$, respectively.

4. Application:
IRIS was developed as a database for consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS do not represent guidelines or standards on their own. IRIS also contains a summary of current American government regulatory actions under various legislative mandates, such as registration under FIFRA as an active ingredient in pesticides, and as a reportable chemical at the 100 pound level under Superfund (CERCLA).

5. Documentation Available:
U.S. EPA, 1995. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington DC.

U.S. EPA, 1987. Assessment of Health Risks to Garment Workers and Certain Home Residents from Exposure to Formaldehyde. U.S. Environmental Protection Agency, Office of Toxic Substances, Washington DC.

U.S. EPA, 1991. Formaldehyde Risk Assessment Update: Final Draft, June 11, 1991. U.S. Environmental Protection Agency, Office of Toxic Substances, Washington DC. 154 p. + appendices.

Key Reference(s):
Kerns, W.D., K.L. Pavkov, D.J. Donofrio, E.J. Gralla and J.A. Swenberg, 1983. Carcinogenicity of Formaldehyde in Rats and Mice After Long-Term Inhalation Exposure. Cancer Res. 43: 4382-4392.

6. Peer Review Process or Public Consultation:
US EPA makes use of peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature, in its assessments. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, both within the US EPA and the Federal Government and without. Information is put on IRIS after the results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:
There is no current US EPA air quality guideline for formaldehyde in ambient air.

8. Key Risk Assessment Considerations:
Formaldehyde is classified as a probable human carcinogen (B2) based on limited evidence in humans and sufficient evidence in animals and other relevant supporting evidence including its known genotoxic activity and the ability to injure cells and affect cell division. Of the 28 epidemiological studies considered by the US EPA in IRIS, three (Blair *et al.*, 1986, 1987, Vaughan *et al.*, 1986a,b, and Stayner *et al.*, 1988) were judged as being well-conducted and capable of detecting small to moderate increases in human cancer risk associated with formaldehyde exposure. Blair *et al.* (1986, 1987) studied occupational exposures at 10 industrial sites and reported statistically significant increases in lung and nasopharyngeal cancer deaths. Although no exposure measurements were taken, Vaughan *et al.* (1988) found a significant association between nasopharyngeal cancer and residing for 10 or more years in a mobile home, especially those from the period of the 1950s to 1970s, a time of increasing formaldehyde-resin usage in building and furnishing materials. In another industrial exposure situation Stayner *et al.* (1988) found increased mortality from buccal cavity tumours in garment workers exposed to formaldehyde.

Despite some reported associations between formaldehyde exposure and increased respiratory tract cancers, the remaining 25 studies were judged by the US EPA to have had limited ability to detect small to moderate increases in formaldehyde risk owing to small sample sizes, small numbers of observed site-specific deaths, and/or insufficient follow-up. Furthermore, these studies were confounded by possible exposures to other carcinogenic agents which may have affected the results.

The US EPA considers that three studies with two strains of rats (both sexes) and one strain of mice (males) represent the principal weight of evidence for classification of formaldehyde as an animal carcinogen in inhalation exposures. In all of these studies (Kerns *et al.*, 1983, Sellakumar *et al.*, 1985, and Tobe *et al.*, 1985), nasal squamous cell carcinomas were found. Additional evidence of respiratory carcinogenicity in other strains and species of mammals (rats, Syrian golden hamsters, and monkeys), as well as evidence of mutagenic/genotoxic activity in a variety

of organisms and cell cultures were considered supportive and was presented in a comprehensive review (Consensus Panel, 1984).

The US EPA considers formaldehyde a genotoxic carcinogen with the absence of a threshold below which effects are not expected to occur. Quantitative assessment was based on the rat carcinogenicity data of Kerns and coworkers (1983). The linearized multistage model (Global 83) was used to estimate carcinogenic potency at low concentrations (well below the actual exposure levels employed in the laboratory experiments), using the airborne concentration as a measure of dose. Extrapolation from animal bioassay data (rats in this case) to humans is based on the species equivalence assumption that a given level of airborne concentration would pose the same cancer risk to all species. A "5-stage" model was found to fit the data adequately, resulting in an upper limit inhalation incremental unit risk estimate of $1.5 * 10^{-2}$ ppm^{-1} ($1.3 * 10^{-5}$ $(\mu g/m^3)^{-1}$) (U.S. EPA, 1987). This corresponds to an additional risk level of 1 in 1,000,000 for a lifetime exposure to 0.08 $\mu g/m^3$ of formaldehyde.

Although not in the IRIS database, a final draft report by EPA (1991) contains a revised estimation approach which incorporates the use of DNA-protein crosslinks as a surrogate measure of formaldehyde delivered dose at the target tissues of the exposed organisms. The linearized multistage procedure (programmed in GLOBAL86) was applied to the rat DNA-protein crosslink levels, adjusted to daily exposure, and the tumour incidence (Kern *et al.* 1983). The modelling procedure yielded a "2-stage" model for best fit. Interspecies extrapolation was based on the assumption that a given level of formaldehyde covalently bound to DNA would impose the same lifetime cancer risk to all species. Using the DNA-protein crosslink airborne concentration relationship for the rats and monkeys, the upper bound lifetime inhalation incremental unit risk (q_1^*) was estimated to be $2.8 * 10^{-3}$ per ppm ($2.3 * 10^{-6}$ $(\mu g/m^{-3})^{-1}$; rat) and $3.3 * 10^{-4}$ ppm^{-1} ($2.8 * 10^{-7}$ $(\mu g/m^{-3})^{-1}$; monkey) for airborne concentration below 0.7 ppm. Since the anatomy and the breathing patterns of humans are closer to monkeys than rats, US EPA considers the monkey a better human surrogate and favours the monkey-based procedure. The monkey-based estimate corresponds to an additional risk level of 1 in 1,000,000 for a lifetime exposure to 3.6 $\mu g/m^3$ of formaldehyde. However, the original 1987 U.S. EPA report remains the basis for the information on the current IRIS database.

9. Key Risk Management Considerations:
None, as no guideline for ambient air currently exists.

10. Multimedia Considerations of Guidelines:
No guideline exists but the risk estimate discussed is for respiratory exposure from air only.

11. Other Relevant Factors.
The experimental exposure range used in the animal experiments is close to that which is expected for some human exposures. Incidence of cancer in male and female animals were similar in the exposure groups where both sexes were tested. The unit risk estimate should not be used where

the air concentration exceeds 800 µg/m^3 since above this concentration the unit risk may not be appropriate.

7.2 Agency-Specific Summary: State of California

1. Name of Chemical: Formaldehyde

2. Agency: State of California (Office of Environmental Health Hazard).

3. Guideline Value(s):
The non-cancer acute reference exposure level for inhalation is 370 $\mu g/m^3$ (based on one hour exposure). The non-cancer chronic reference exposure level for inhalation is 3.6 $\mu g/m^3$. The cancer potency unit risk value (the probability of contracting cancer with constant exposure to an ambient air concentration of 1 $\mu g/m^3$ over 70 years) is $6.0 * 10^{-6}$ $(\mu g/m^3)^{-1}$ (California EPA, 1992b). This corresponds to a risk of 1 in 1,000,000 for a 70 year exposure to a formaldehyde concentration of 0.17 $\mu g/m^3$.

Cancer and chronic non-cancer reference exposure levels should be compared with modelled annual average air concentrations while acute non-cancer reference levels should be compared with modelled 1-h average concentrations.

4. Application:
"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' Program." (CAPCOA, 1993). This program is based on a California State law, the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 et seq.). The act specifies how local Air Pollution Control Districts determine which facilities in their area will prepare a health risk assessment, how such health risk assessments should be prepared, and how the results are to be prioritized. These guidelines were prepared to provide consistent risk assessment methods and report presentation to: 1) compare one facility against another, 2) expedite the review of risk assessments by reviewing agencies, and 3) minimize revisions and resubmission of risk assessments. The various health-based exposure levels developed for and employed in this program should not be used outside the framework of the program. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. Documentation Available:
CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association (CAPCOA).

California EPA, 1992. Final Report on the Identification of Formaldehyde as a Toxic Air Contaminant. Part A Exposure Assessment. Technical Support Document. California Environmental Protection Agency, Air Resources Board, Sacramento CA. 89 p. + appendices.

California EPA, 1992. Final Report on the Identification of Formaldehyde as a Toxic Air Contaminant. Part B Health Assessment. Technical Support Document. California Environmental Protection Agency, Air Resources Board, Sacramento CA. 25 p. + appendices.

Key Reference(s):

Kerns, W.D., K.L. Pavkov, D.J. Donofrio, E.J. Gralla and J.A. Swenberg, 1983. Carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure. Cancer Res. 43: 4382-4392.

US EPA, 1987. Assessment Of Health Risks To Garment Workers And Certain Home Residents From Exposure To Formaldehyde. U.S. Environmental Protection Agency, Risk Assessment Branch, Office of Toxic Substances. (Note: Key information is also presented in the IRIS database and the reader is referred to that source).

Lewis D.C. and G.V. Alexeeff, 1989. Quantitative Risk Assessment of Non-cancer Health Effects for Acute Exposure to Air Pollutants IN: Proceedings of the Air and Waste Management Association 82nd Annual Meeting. June 1989, Vol. 89-91. 4 p.

6. Peer Review Process or Public Consultation:

Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA) using peer-reviewed scientific research data. Both the exposure and health assessments have undergone public review and comment prior to finalization. Under the CAPCOA risk assessment process, each assessment is site-specific and public notice to all exposed individuals is required when the assessment concludes that a significant health risk is associated with emissions from a facility. Public input is obtained in identifying and ranking areas and facilities for risk assessment screening. Further additional input is expected as the process moves forward.

7. Status of Guideline:

Current, but updates using the new California risk assessment guidelines are being considered in the California Senate.

8. Key Risk Assessment Considerations:

The non-cancer acute reference exposure level for inhalation of 370 $\mu g/m^3$ is based on human respiratory irritation using the Defined Practical Threshold (DPT) methodology proposed by Lewis and Alexeeff (1989), which employs the 95% lower confidence estimate on a concentration for a 1% response incidence. The DPT was estimated as 0.25 ppm and a time adjustment factor of 1.73 was applied to obtain a reference value of 0.4 ppm (370 $\mu g/m^3$). This value should protect against perceptible occurrence of observable effects, including irritation, among an exposed human population for a one hour exposure.

The non-cancer chronic reference exposure level for inhalation is 3.6 $\mu g/m^3$. Non-cancer chronic reference limits are derived from reference and occupational limits (IRIS and ACGIH TLVs). In this case, a TLV of 1 ppm was divided by an uncertainty factor of 420. The uncertainty factor was derived by taking a factor of 4.2 to extrapolate a 40 hour work week to an 160 hour full week, a factor of 10 to account for the fact that adverse health effects are sometimes seen at the TLV level, and an additional factor of 10 to extrapolate from healthy workers to sensitive members of the public.

California agrees with the US EPA contention that formaldehyde is a genotoxic carcinogen with no threshold for its effects and that the linear multistage model approach provides a valid high-to-low dose extrapolation method. The extrapolation from animal bioassay data to humans was performed with the acknowledgement that evidence of carcinogenic activity at low doses in humans was "very limited". Although California used the same animal bioassay data (Kerns *et al.*, 1983), the same measure of dose (DNA-protein crosslink levels) and model (Global 86) as the U.S. EPA (1991), they considered a "3 stage" model yield the best fit to the tumour data. Interspecies extrapolation based on body surface area scaling factor (1.2) gave an upper bound lifetime inhalation unit risk of $7 * 10^{-3}$ ppm^{-1} or $6.0 * 10^{-6}$ $(\mu g/m^3)^{-1}$. California has tried to incorporate the effect of nasal cell proliferation in the modelling but concluded that those calculations were not well enough established to give a good result.

9. Key Risk Management Considerations:
The exposure guidelines were prepared for both non-cancer and cancer-based endpoints. The cancer-based value is used in a screening risk assessment to determine the maximum offsite cancer risk for the exposed human population. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

The State of California allows local options to address the possible economic impacts of formaldehyde emission control. It appears that the options are under local control and are based on local risk, socioeconomic analyses and feedbacks from public workshops and hearings. The enforcement mechanism is via operating permits. Thus, the process is primarily directed towards site-specific evaluations and development of further regulatory tools rather than towards enforceable levels in themselves.

10. Multimedia Considerations of Guidelines:
The California EPA specified that non-inhalation pathways should be considered in the exposure modelling process for a number of substances (specified in Table III-5 in CAPCOA, 1993). However, formaldehyde is not among them. The California EPA did acknowledge that exposure pathways other than air (i.e. water and food) were possible for formaldehyde, but that, due to the lack of quantitative information and the predominance of airborne exposure, other exposure pathways were not considered in the assessment.

11. Other Relevant Factors.

Indoor air exposure, which was found to be much greater than outdoor exposure, was considered in the exposure assessment. Outdoor air exposure was estimated to average about 5.4 $\mu g/m^3$, (range: 3.9-6.3 $\mu g/m^3$) for various areas of the state.

7.3 Agency-Specific Summary: World Health Organization

1. Name of Chemical: Formaldehyde

2. Agency: World Health Organization

3. Guideline Value(s):
The guideline value is a time-weighted average of 100 µg/m^3 over an averaging period of 30 minutes. For the case of specially sensitive groups within the general population that show hypersensitivity reactions without immunological signs, WHO recommends that the formaldehyde concentration should be kept at a minimum and should not exceed 10 µg/m^3 (as a ½ hour average).

4. Application:
"The guidelines are intended to provide background information and guidance to governments in making risk management decisions, particularly in setting standards. It should be strongly emphasized that the guideline values are not to be regarded as standards in themselves" (WHO, 1987, pg xiii)

5. Documentation Available:
World Health Organization (WHO), 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark. 426 p.

WHO, 1996. Updating and Revision of the Air Quality Guidelines for Europe. Report on a WHO Working Group on Volatile Organic Compounds, Brussels, Belgium, 2-6 October, 1995. WHO Regional Office for Europe, Denmark. 22p.

Key Reference(s):
Consensus Panel, 1984. Report on the Consensus Workshop on Formaldehyde. Environ. Health Perspect. 58:323-381.

6. Peer Review Process or Public Consultation:
Scientific background documents were prepared by experts and submitted to working groups consisting of international experts to provide a basis for discussion. After a series of meetings and internal and external reviews by experts and representatives of the Member States of the Region, the resultant conclusions and recommendations were presented at a final meeting where they were adopted by consensus of the representatives. In addition, peer-reviewed scientific research data were employed in the development of these documents.

7. Status of Guideline:
Current.

8. Key Risk Assessment Considerations:

Formaldehyde is an irritant to the eyes, nose and throat, resulting in concentration-dependent discomfort. Humans vary in the degree of their responses to formaldehyde. Generally, significant increases in signs of irritation occur at levels above 100 $\mu g/m^3$ in healthy subjects. A progression of symptoms and effects occur at concentrations above 1.2 mg/m^3.

Formaldehyde was first examined by IARC in 1982. The working group concluded that there was sufficient evidence of carcinogenicity in animals, but the human evidence was inadequate for assessing carcinogenicity of formaldehyde in humans. IARC revisited the literature in 1987 and classified formaldehyde as a Group 2A carcinogen (sufficient evidence in animals, limited evidence in humans) and reaffirmed its evaluation in 1995. WHO considers the estimation of human carcinogenic risk for formaldehyde from animal data a matter of great uncertainty because the dose response curve is nonlinear, the risk being disproportionately low at low concentrations. It also appears that the dose response curves were nearly identical for neoplastic changes, cell turnover, DNA-protein cross-links and hyperproliferation, when the relationship between nonneoplastic and neoplastic lesions in the nasal respiratory epithelium were analysed. This information suggests an association among the observed cytotoxic, genotoxic and carcinogenic effects. It is likely that hyperproliferation induced by cytotoxicity plays a significant role in the formation of nasal tumours by formaldehyde in the rat. Although the anatomy and physiology of the respiratory tract between rats and humans are different, their respiratory tract defence mechanisms are similar. WHO considers it reasonable to assume the human response to formaldehyde to be similar to that of the rat. Therefore, if the respiratory tract tissue is not repeatedly damaged, exposure to humans to low, non-cytotoxic concentrations of formaldehyde can be assumed to be associated with a negligible cancer risk. WHO considers this assumption to be consistent with epidemiological findings of excess risks of nasopharyngeal and sinonasal cancers at concentrations above approximately 1 mg/m^3.

WHO recommended an air quality guideline value of 100 $\mu g/m^3$ to prevent sensory irritation in the general population. Since the recommended value is more than one order of magnitude lower than a presumed threshold for cytotoxic damage to the nasal mucosa, this guideline value is considered sufficiently low to protect humans from any significant risk of upper respiratory tract cancer.

9. Key Risk Management Considerations

The basis of the guideline is odour/irritation. The recommended guideline is lower than the presumed threshold for cytotoxic damage to the nasal epithelium. Since it is likely that cytotoxicity plays a significant role in the formation of nasal tumour, the guideline value is considered protective of humans against any significant upper respiratory cancer risk. In order to avoid the complaints of specially sensitive people, the formaldehyde concentration should be kept below 10 $\mu g/m^3$ as a 30-minute average.

10. Multimedia Considerations of Guidelines:
Human exposure from air, drinking water, and diet was considered in the evaluation but this did not specifically contribute to the determination of the final guideline value.

11. Other Relevant Factors.
The guideline value is applicable to both indoor and outdoor situations.

7.4 Agency-Specific Summary: The Netherlands

1. Name of Chemical: Formaldehyde

2. Agency: Netherlands Ministry of Housing, Spatial Planning and the Environment

3. Guideline Value(s):
National air limit values (not to be exceeded) are 100, 40, and 30 µg/m^3 for an hourly average (99.99 percentile), a 24-h average (98 percentile), and a 24-h average (95 percentile), respectively. In addition, there is a maximum limit value of 120 µg/m^3 for formaldehyde in building interiors.

4. Application:
Limit values are non-statutory environmental quality objectives that are considered policy guidelines. They should not be exceeded and are requirements that must be met. These effect-oriented guidelines may be used simultaneously with source-oriented emission criteria, which are the primary regulatory mechanism. If effects-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effects-oriented guidelines.

5. Documentation Available:
Netherlands MHSPE, 1994. Environmental Quality Objectives in the Netherlands. A review of environmental quality objectives and their policy framework in the Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 p.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulations Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

Note: Earlier air criteria documents or more recent integrated criteria documents are available for priority substances such as formaldehyde but only in Dutch.

6. Peer Review Process or Public Consultation:
No specific information on this issue was presented in the available English documentation.

7. Status of Guideline:
Current.

8. Key Risk Assessment Considerations:
Formaldehyde is considered to be a carcinogen by the Dutch government which recognizes the IARC (1987) classification of formaldehyde as a group 2A carcinogen (limited proof for humans and sufficient proof for laboratory animals). As such, it has been placed on a priority list of

chemicals (SAC) requiring special attention. An integrated criteria document, which contains all relevant data needed to determine any risk, has been prepared but these documents are only available in Dutch. It appears from inspection of documentation available in English that recommended air limits are based on consideration of irritation and/or odour, rather than carcinogenicity.

9. Key Risk Management Considerations:
National limit values include consideration of environmental, economic, and social interests as well as technical options. Specific information on such details was not presented in the available documentation.

10. Multimedia Considerations of Guidelines:
Multimedia exposure was not considered in the development of the current air guideline limits. However, inter-compartmental criteria which address this problem are being developed. A specific schedule for revisions based on this process has not been announced and formaldehyde is not on the initial list of chemicals to be considered.

11. Other Relevant Factors:
No information.

7.5 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. Name of Chemical: Formaldehyde

2. Agency: The values reported below are those recommended by the Swedish Institute of Environmental Medicine. According to Dr. K. Victorin of the Swedish Institute of Environmental Medicine (personal communication), no official Swedish air quality guidelines have been promulgated by the Swedish Environmental Protection Agency.

3. Guideline Value(s):
Air concentrations of formaldehyde should not exceed 120 µg/m^3 for short-term exposures and 12-60 µg/m^3 for long-term exposures. Since specific averaging times are not indicated, short-term exposure will be assumed to represent an averaging time of one hour and long-term exposure an averaging time of one year. The report in English translation only provides the recommended guidelines and a three line summary of the rationale but not any supporting information.

4. Application:
Used on an *ad hoc* basis.

5. Documentation Available:
Victorin, K., 1993. Health Effects of Urban Air Pollutants: Guideline Values and Conditions in Sweden. Chemosphere 27:1691-1706.

Note: Although documentation in Swedish has been prepared, no English version is available.

6. Peer Review Process or Public Consultation:
No information is available in the documentation.

7. Status of Guideline:
It has no official status but has been used on an *ad hoc* basis by Swedish regulators.

8. Key Risk Assessment Considerations:
The recommended short-term value was set at the threshold for irritation while the long-term value was generated by applying a 10-fold safety factor to the short-term guideline.

9. Key Risk Management Considerations:
The recommended long-term guideline value is regarded to pose low carcinogenic risk to humans.

10. Multimedia Considerations of Guidelines:
Based on human health considerations for respiration only.

11. Other Relevant Factors.

No information.

7.6 Agency-Specific Summary: New York State

1. Name of Chemical: Formaldehyde

2. Agency: New York State

3. Guideline Value(s):
The recommended 1-h average air concentration is 30 µg/m^3. The recommended annual average is 0.06 µg/m^3.

4. Application:
"... they are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212 and 257." (p. 1, NY DEC, 1991.) These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. Rather than being employed as legally enforceable ambient air quality standards, the guidelines are used to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate, and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. Documentation Available:
New York State DEC, 1991. New York State Air Guideline-1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation (DEC), Albany, New York NY. 20 p. + Appendices.

New York State DOH, 1990. Formaldehyde Health Assessment. Division of Environmental Health, Bureau of Toxic Substance Assessment (Note: only report cover letter available to date).

6. Peer Review Process or Public Consultation:
The scientific documents prepared by New York State employed peer reviewed data and models as well as professional judgement of its scientific staff. There are opportunities for public comment on guidelines and the guideline development process, but specific information on the process for formaldehyde was not presented in the available documentation.

7. Status of Guideline:
Current.

8. Key Risk Assessment Considerations:
The 1-h average guideline was derived by dividing the no-observed effect level of 300 µg/m^3 (based on a reduction in nasal mucous flow, the most sensitive objective response to respiratory

irritation) by a factor of 10. It is not expected that short-term exposures at this level will produce complaints of eye, nose or throat irritation above that encountered with background air exposures.

The recommended annual average guideline of 0.06 $\mu g/m^3$ is based on a lifetime cancer risk estimate of 1 in 1,000,000. Although the detailed NY Department of Health document is not available, it is expected that the carcinogenicity data and evaluation techniques used in the assessment are similar to those employed by other agencies in the USA.

9. Key Risk Management Considerations
The 1-h value of 30 $\mu g/m^3$ should not be used as an incremental concentration above non-industrial background because of the potential for irritation.

Based on the toxicity classification system developed by New York State, formaldehyde is classified as a high toxicity compound. The New York State has adopted the IARC and US EPA classification of carcinogenic chemicals and its cancer-based guidelines use a lifetime risk probability of 1 in 1,000,000. It is acknowledged that, although there is evidence that formaldehyde is carcinogenic to rats and mice, epidemiology provides only limited evidence for carcinogenicity in humans.

Specific computer model and guidance manual are provided for the use of the guidelines in impact screening in the permitting process. The latest version of Appendix B of the New York State Air Guide-1 is dated April 4, 1994.

10. Multimedia Considerations of Guidelines:
Considers human airborne exposure only.

11. Other Relevant Factors.
Odour detection values may be used to evaluate acceptable short-term impacts but, as a general rule, modelled odour information should not be used exclusively or quantitatively in the evaluation, since nuisance odours tend to be both subjective and variable in nature.

7.7 Agency-Specific Summary: State of Massachusetts

1. Name of Chemical: Formaldehyde

2. Agency: Commonwealth of Massachusetts

3. Guideline Value(s):
The 24-h ceiling limit is 0.33 µg/m^3 (0.27 ppb), based on the threshold effects exposure limit. The allowable ambient limit (AAL) is 0.08 µg/m^3 (0.06 ppb) for an annual (1 year) averaging time and is based on consideration of carcinogenic effects.

4. Application:
"... the Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance, and enforcement components of the Commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, pg. ix). The primary goal is to "protect the public health and welfare from any air contaminant causing known or potentially injurious effects". The ambient air levels developed in this process should not be considered legally enforceable air quality standards since they deal only with health-related matters and contain no consideration for technological, economic, or enforcement concerns. Rather, they should be employed as guidelines in the development of subsequent regulatory action which takes into consideration all relevant concerns.

5. Documentation Available:
Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston MA.

Key Reference(s):
ACGIH, 1986. Documentation Of The Threshold Limit Values for Substances in Workroom Air (5th ed.). American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH.

Swenberg, J.A., W.D. Kerns, R.I. Mitchell, E.J. Gralla, and K.L. Pavkov, 1980. Induction of Squamous Cell Carcinomas of the Rat Nasal Cavity by Inhalation Exposure to Formaldehyde Vapor. Cancer Res. 40:3398-3402.

Kerns, W.D., K.L. Pavkov, D.J. Donofrio, E.J. Gralla, and J.A. Swenberg, 1983. Carcinogenicity of Formaldehyde in Rats and Mice after Long-Term Inhalation Exposure. Cancer Res. 43:4382-4392.

U.S. EPA, 1987. Assessment of Health Risks to Garment Workers and Certain Home Residents from Exposure to Formaldehyde. U.S. Environmental Protection Agency, Office of Toxic

Substances, Washington DC. (Note: Massachusetts used the 1985 draft rather than the 1987 final version of this document in their assessment. The information is also presented in the IRIS database.)

6. Peer Review Process or Public Consultation:
Peer-reviewed scientific research data, analyses, and evaluations from various sources, including a variety of public and government agencies from around the world and the published scientific literature, were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (ARC), the American National Toxicology Program (NTP), and the U.S. EPA was used. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to. However, external peer reviews on the Massachusetts methodology and guideline document have been carried out and public input was solicited at least two public meetings (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication).

7. Status of Guideline: Current.
Although guideline values are periodically updated, revisions to the current value for formaldehyde are not under consideration (D. Manganaro, Massachusetts Department of Environmental Protection, personal communication).

8. Key Risk Assessment Considerations:
A regulation development system incorporating adjustments for exposure and a number of safety factors to address various types of uncertainties were generated both for carcinogens and non-carcinogens.

The 24-h ceiling limit of 0.33 $\mu g/m^3$ is based on the threshold effects exposure limit (TEL) methodology. The TEL is derived from the most appropriate occupational limit (MAOL) among the exposure limits proposed by NIOSH, ACGIH, and OSHA. In this case, the most appropriate limit was developed by ACGIH. The initial MAOL of 1230 $\mu g/m^3$ was divided by 4.2 to adjust for exposure from a 40-h week to a continuous 168-h week, by a factor of 1.75 to extrapolate from an adult to a child, and by a factor of 10 to account for the uncertainty associated with high risk groups. Since the toxicity data was judged to be adequate, an additional uncertainty factor of 10 was not applied. This generated an adjusted MAOL of 13.61 ppb. The final TEL was obtained by dividing the adjusted MAOL by a threshold effect uncertainty factor (TEUF) of 10, and adjusting to an assumed air source factor of 20% (ambient air is assumed to represent 20% of the total exposure).

The allowable ambient limit (AAL) is 0.08 $\mu g/m^3$ (0.06 ppb) for an annual (1 year) averaging time, corresponding to an excess cancer risk of $1*10^{-6}$ for a lifetime exposure based on a unit risk value of $1.3*10^{-5}$ $(\mu g/m^3)^{-1}$. The unit risk value was adopted from U.S. EPA (1985). See the IRIS discussion in Section 5.1 for a review of the development of this value.

9. Key Risk Management Considerations:
The primary objective of the process is the protection of public health. The Massachusetts system uses hazard assessment only and does not use the number of exposed individuals as a criterion for regulatory action. Furthermore, the selection of the AAL is based on the most sensitive effect. The U.S. EPA's cancer unit risk values (EPA, 1985) and the ACGIH occupational TLV values were adopted for regulation development purposes. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical is set at one in a million ($1*10^{-6}$) for a 70 year lifetime duration.

10. Multimedia Considerations of Guidelines:
A generic allowance was made for contributions from sources other than air. "A relative source contribution factor of 20% is also included to account for sources other than air." (Commonwealth of Massachusetts, 1990, pg viii).

11. Other Relevant Factors.
"Because formaldehyde is reactive and causes effects at the site of deposition, the carcinogenic potency calculated for inhalation exposure should not be used for other routes of exposure." (Commonwealth of Massachusetts, 1990, Volume II, pg. E-52).

The document notes that there is a controversy concerning the cancer data for formaldehyde. Specifically, the animal data show a nonlinear response at the higher dose levels employed, suggesting that a threshold exists. Furthermore, it is acknowledged that the linear multistage extrapolation model substantially overestimates the true cancer risk of formaldehyde. However, since the controversy had not been resolved by the time the guidelines came into force, a commitment was made to revise the cancer AAL whenever a new consensus opinion was reached.